REMARKS

1. Rejection of claims 1-7 and 9-11 under 35 U.S.C. § 103(a)

The Official Action states that claims 1-7 and 9-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Terahara *et al*. (CA 2428181).

RESPONSE

Applicants respectfully traverse this rejection of claims 1-7 and 9-11. The cited reference does not establish a *prima facie* case of obviousness against the presently pending claims. To establish a prima facie case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court recently held in KSR International Co. v. Teleflex Inc. et al., Slip Opinion No. 04-1350, 550 U.S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it

can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (KSR, supra, slip opinion at 13-15). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Amgen Inc. v. Chugai Pharm. Co., 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

Further, the Supreme Court in KSR reiterated the framework for determining obviousness that was stated in Graham v. John Deere Co. 383 U.S. 1, 148 USPQ 459 (1966). The four factual inquiries that were recited in Graham are as follows: (1) Determining the scope and contents of the prior art; (2) Ascertaining the differences between the prior art and the claims in issue; (3) Resolving the level of ordinary skill in the pertinent art; and (4) Evaluating evidence of secondary

considerations, such as unexpected results. Id. As stated in **MPEP 2141**, secondary considerations such as unexpected results must be considered in every case in which they are present.

A. The Presently Claimed Invention

The presently claimed invention as exemplified by claim 1 is directed to:

> A patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive base agent and pergolide and/or a pharmaceutically acceptable salt thereof, wherein the adhesive base agent comprises an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties and a rubber polymer, and a weight ratio of the content of the acrylic polymer to the content of the rubber polymer is from 1:1 to 1:19.

B. The Teachings of the Terahara *et al.* Reference

The Terahara *et al.* reference describes a "transdermal preparation containing a polymer compound having amino groups, a drug forming an acid addition salt, and carboxylic acid and/or a salt thereof, characterized in that the content of the polymer compound having amino groups is 50% or less by weight based on the whole preparation, and a molar ratio of the amino groups in the polymer compound is 0.5 mol or higher per mol of the drug, and the content of the carboxylic acid and/or the salt thereof is 1 to 10 mol per mol of the sum of the drug and the amino groups in the polymer compound." See p. 5, lines 10-19 of

Terahara *et al.* See p. 5, lines 10-19 of Terahara *et al.*

C. No *prima facie* Case of Obviousness has Been Shown by the Examiner

The Terahara *et al.* reference does not describe the specific combination of components recited in the presently pending claims as required by In re Wilson, 165 USPQ 494, 496, and, therefore, cannot render claims 1-7 and 9-11 obvious. In particular, Terahara *et al.* does not disclose the combination of "pergolide and/or a pharmaceutically acceptable salt thereof", "an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties and a rubber polymer, and a weight ratio of the content of the acrylic polymer to the content of the rubber polymer is from 1:1 to 1:9." On page 4 of the Official Action, the Examiner asserts that Terahara *et al.* in Example 5 discloses a formulation containing pergolide mesilate, an acrylate polymer, a rubber (SIS) and alicyclic saturated hydrocarbon resin. However, the acrylate polymer disclosed in Example 5 of Terahara *et al.* is not "an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties," as required by the presently pending claims. Specifically, the acrylate polymer

disclosed in Example 5 of Terahara *et al.* is "Duro-Tak 387-2287," which is an acrylate polymer having hydroxyl groups. Accordingly, the Terahara *et al.* reference does not teach or suggest the combination of components as presently claimed. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness.

D. The Unexpectedly Superior Properties of the Claimed Matrix

As stated in **MPEP 716.02**, the rationale to support a conclusion that the claims would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. Accordingly, Applicants' data submitted in the present specification shows unexpected, and thus unpredictable results for the formulations comprising the claimed components.

Applicants kindly bring the Examiner's attention to the unexpectedly superior properties of the presently claimed matrix outlined in Tables 1-3 on pages 33-35 of the instant specification. The data clearly shows enhanced maximum skin permeation rates for the drug pergolide in those examples that

contain all the components as recited in the presently pending claims when compared to prior art examples where one or more of the claimed components are not present in the composition. In particular, Examples 1-6 summarized in Table 1 show drug permeation rates per unit area of skin for compositions containing the presently claimed components. Comparative Examples 1-10 in Tables 2 and 3 show drug permeation rates for compositions lacking at least one of the components of the presently claimed formulation. The data clearly shows superior skin permeation rates and patch properties, when compared to the drug permeation rates for compositions lacking at least one of the claimed components.

Accordingly, the results outlined in Tables 1-3 on pages 33-35 of the instant specification show unexpectedly superior results for the compositions as presently claimed. As such, the presently pending claims are not obvious over the cited prior art reference. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-7 and 9-11.

2. Rejection of claims 1 and 4-11 under 35 U.S.C. § 103(a)

The Official Action states that claims 1 and 4-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over

Chono *et al.* (EP 1201232) in view of Hirano *et al.* (US 2002/0102290).

RESPONSE

Applicants respectfully traverse this rejection of claims 1 and 4-11. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims. The requirements for establishing a *prima facie* case of obviousness, as previously discussed in Section 1, are incorporated herein by reference in their entirety.

A. The Presently Claimed Invention

As previously discussed, the presently claimed invention as exemplified by claim 1 is directed to:

> A patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive base agent and pergolide and/or a pharmaceutically acceptable salt thereof, wherein the adhesive base agent comprises an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties and a rubber polymer, and a weight ratio of the content of the acrylic polymer to the content of the rubber polymer is from 1:1 to 1:19.

B. The Teachings of the Chono *et al.* Reference

The Chono *et al.* reference describes a patch formulation comprising a basic drug, an adhesive layer, and a backing layer for supporting the adhesive layer.

C. The Teachings of the Hirano *et al.* Reference

The Hirano *et al.* reference describes a "percutaneous therapeutic apparatus having at least three (3) layers comprising a medicine non-permeable backing layer, a medicine storage layer containing serotonin-receptor antagonist between said backing layer and medicine-releasing layer, and a pressure-sensitive adhesive layer which is able to control release of medicine." See p. 11 of Hirano *et al.*

D. No *prima facie* Case of Obviousness has Been Shown by the Examiner

Neither the Chono *et al.* nor Hirano *et al.* references describe any examples containing the combination of components recited in the presently pending claims, namely "pergolide and/or a pharmaceutically acceptable salt thereof, an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties and a rubber polymer, and a weight ratio of the content of the acrylic polymer to the content of the rubber polymer is from 1:1 to 1:9." Further, Chono *et al.* does not teach or suggest the use of pergolide in combination with the polymers as presently pending claimed.

Nowhere in the secondary Hirano *et al.* reference is the use

of pergolide described. On page 5 of the Official Action, the Examiner asserts that Example 1 in Hirano *et al.* discloses a formulation containing a "pressure-sensitive adhesive comprising an acrylate polymer (2-ethylhexyl acrylate-vinyl acetate copolymer) and a rubber polymer (polyisobutylene and styrene/isoprene/styrene block copolymer." However, the drug used in Example 1 in Hirano *et al.* is ondansetron hydrochloride, a serotonin-receptor antagonist, and not the drug pergolide as presently claimed.

Accordingly, neither the Chono *et al.* nor the Hirano *et al.* reference describe all the limitations of the presently pending claims. As such, the Examiner has failed to establish a *prima facie* case of obviousness.

E. The Unexpectedly Superior Properties of the Claimed Matrix

As stated in **MPEP 716.02**, the rationale to support a conclusion that the claims would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. Accordingly, Applicants' data submitted in the

present specification shows unexpected, and thus unpredictable results for the formulations comprising the claimed components.

Applicants kindly bring the Examiner's attention to the unexpectedly superior properties of the presently claimed matrix outlined in Tables 1-3 on pages 33-35 of the instant specification. The data clearly shows enhanced maximum skin permeation rates for the drug pergolide in those examples that contain all the components as recited in the presently pending claims when compared to prior art examples where one or more of the claimed components are not present in the composition. In particular, Examples 1-6 summarized in Table 1 show drug permeation rates per unit area of skin for compositions containing the presently claimed components. Comparative Examples 1-10 in Tables 2 and 3 show drug permeation rates for compositions lacking at least one of the components of the presently claimed formulation. The data clearly shows superior skin permeation rates and patch properties, when compared to the drug permeation rates for compositions lacking at least one of the claimed components.

Accordingly, the results outlined in Tables 1-3 on pages 33-35 of the instant specification show unexpectedly superior results for the compositions as presently claimed. As such, the

presently pending claims are not obvious over the cited prior art references. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1 and 4-11.

3. Rejection of claims 2 and 3 under 35 U.S.C. § 103(a)

The Official Action states that claims 2 and 3 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chono *et al.* in view of Hirano *et al.* and further in view of Terahara *et al.*

RESPONSE

Applicants respectfully traverse this rejection of claims 2 and 3. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims. The requirements for establishing a *prima facie* case of obviousness, as previously discussed in Section 1, are incorporated herein by reference in their entirety.

A. The Presently Claimed Invention

As previously discussed, the presently claimed invention as exemplified by claim 1 is directed to:

> A patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive base agent and pergolide and/or a pharmaceutically acceptable salt thereof, wherein the adhesive base agent comprises an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties and a rubber polymer, and a weight ratio of

the content of the acrylic polymer to the content of the rubber polymer is from 1:1 to 1:19.

Dependent claim 2 incorporates the features recited in independent claim 1, and further recites the adhesive base agent as comprising "a basic nitrogen-including polymer including a basic nitrogen and having no self-adhesion property."

Claim 3 is dependent upon claim 2 and recites that "the basic nitrogen-including polymer is at least one kind selected from methyl methacrylate - butyl methacrylate - dimethylaminoethyl methacrylate terpolymer and polyvinyl acetal diethylamino acetate."

B. The Teachings of the Chono *et al.* Reference

The Chono *et al.* reference describes a patch formulation comprising a basic drug, an adhesive layer, and a backing layer for supporting the adhesive layer.

C. The Teachings of the Hirano *et al.* Reference

The Hirano *et al.* reference describes a percutaneous therapeutic apparatus having at least three (3) layers comprising a medicine non-permeable backing layer, a medicine storage layer containing serotonin-receptor antagonist between said backing layer and medicine-releasing layer, and a pressure-

sensitive adhesive layer which is able to control release of medicine.

D. The Teachings of the Terahara *et al.* Reference

The Terahara *et al.* reference describes a transdermal preparation containing a polymer compound having amino groups, a drug forming an acid addition salt, and carboxylic acid and/or a salt thereof, characterized in that the content of the polymer compound having amino groups is 50% or less by weight based on the whole preparation, and a molar ratio of the amino groups in the polymer compound is 0.5 mol or higher per mol of the drug, and the content of the carboxylic acid and/or the salt thereof is 1 to 10 mol per mol of the sum of the drug and the amino groups in the polymer compound.

E. No *prima facie* Case of Obviousness has Been Shown by the Examiner

Neither the Chono *et al.* nor the Hirano *et al.* references describe a "basic nitrogen-including polymer including a basic nitrogen and having no self-adhesion property" as recited in presently pending claim 2. Further, the Terahara *et al.* reference teaches the use of an acrylate polymer, "Duro-Tak 387-2287," having hydroxyl groups and therefore differs from the presently claimed transdermal patch formulation which requires

"an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties." Accordingly, there is no teaching anywhere in the cited prior art references to arrive at the combination of components recited in the presently pending claims, namely pergolide and/or a pharmaceutically acceptable salt thereof, an acrylic polymer including no substantial carboxyl group and hydroxyl group in the molecule and having self-adhesion properties and a rubber polymer, and a weight ratio of the content of the acrylic polymer to the content of the rubber polymer is from 1:1 to 1:9. As such, the presently pending claims are not obvious over the cited prior art references. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 2 and 3.

F. The Unexpectedly Superior Properties of the Claimed Matrix

As stated in **MPEP 716.02** and previously discussed in Sections 1 and 2, the rationale to support a conclusion that the claims would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of

ordinary skill in the art at the time of the invention. Accordingly, Applicants' data submitted in the present specification shows unexpected, and thus unpredictable results for the formulations comprising the claimed components.

Applicants kindly bring the Examiner's attention to the unexpectedly superior properties of the presently claimed matrix outlined in Tables 1-3 on pages 33-35 of the instant specification. The data clearly shows enhanced maximum skin permeation rates for the drug pergolide in those examples that contain all the components as recited in the presently pending claims when compared to prior art examples where one or more of the claimed components are not present in the composition. In particular, Examples 1-6 summarized in Table 1 show drug permeation rates per unit area of skin for compositions containing the presently claimed components. Comparative Examples 1-10 in Tables 2 and 3 show drug permeation rates for compositions lacking at least one of the components of the presently claimed formulation. The data clearly shows superior skin permeation rates and patch properties, when compared to the drug permeation rates for compositions lacking at least one of the claimed components.

Accordingly, the results outlined in Tables 1-3 on pages

33-35 of the instant specification show unexpectedly superior results for the presently claimed compositions. As such, the presently pending claims are not obvious over the cited prior art references. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 2 and 3.

4. Provisional Rejection of Claim 1 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

The Official Action states that claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8 and 12 of copending U.S. Patent Application Serial No. 10/469,612.

Applicants respectfully request that the Examiner hold this rejection in abeyance until such time as the Examiner indicates there is successful resolution of the claim rejections noted above. Applicants, at that time, will either address the rejection or file a terminal disclaimer over copending U.S. Patent Application No. 10/469,612.

CONCLUSION

Based upon the above remarks, it is submitted that the presently claimed subject matter is in condition for immediate allowance. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,
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